Remarks

Claims 13-31 were pending in the subject application. By this Amendment, claim 25 has been amended, claims 13-24, 26, and 29-31 have been cancelled, and new claims 32-46 have been added. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 25, 27, 28, and 32-46 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

The applicants and the applicants' representative wish to thank Examiner Duffy for the courtesy of the telephonic interview conducted with the undersigned on October 18, 2004, regarding claims 25-29 and the rejections under 35 U.S.C. §112, first and second paragraphs, and 35 U.S.C. §102(b). The remarks and amendments set forth herein are consistent with the substance of the interview and are believed to address the outstanding issues as discussed during the interview.

The Examiner has acknowledged the applicants' claim of foreign priority based on British applications GB 9828346.8 and GB 9908321.4 but indicates that certified copies were not filed. The applicants note that certified copies of the priority documents were included with the PCT application as transmitted to the Patent Office by WIPO. Attached is a copy of form PCT/IB/304, confirming that the priority documents were included with the PCT application.

The Examiner has indicated that the title of the invention is not descriptive and that a new title is required that is clearly indicative of the invention to which the claims are directed. The applicants have amended the title of the invention to "NADP-dependent Glyceraldehyde-3-phosphate Dehydrogenase For Therapeutic Use" which more clearly indicates the claims to which the invention is directed. Accordingly, reconsideration and withdrawal of this objection is respectfully requested.

By this Amendment, claim 25 has been amended to recite a method for the treatment or prevention of a Group B *Streptococcal* infection, wherein said method comprises administering to a patient in need of such treatment or prevention, an immunologically effective amount of an isolated bacterial NADP-dependent glyceraldehydes-3-phosphate dehydrogenase. Support for this amendment can be found, for example, at page 2, lines 3-4; page 3, lines 9-12; page 4, lines 10-15 and 20-26; and page 10, lines 18-26, of the specification. Claims 32-46 have been added. Support

for claims 35 and 40 can be found, for example, at page 10, lines 22-24, of the specification. Support for claims 32 and 43 can be found, for example, at page 2, lines 27-30, and page 10, lines 18-21, of the specification. Support for claims 33, 34, 41, and 42 can be found, for example, at page 2, lines 11-15 and 27-30, and page 3, lines 20-29, of the specification. Support for claims 36, 44, and 46 can be found, for example, at page 3, lines 13-18, of the specification. Support for claim 37 can be found, for example, at page 2, lines 3-4 and 11-16; page 3, lines 9-12; page 4, lines 6-15; and page 10, lines 18-26, of the specification. Support for claims 38 and 39 can be found, for example, at page 1, lines 21-33, of the specification, and claims 10 and 11 as originally filed. Support for claim 43 can be found, for example, at page 2, lines 17-22 and 27-30, and page 4, lines 10-15, of the specification. Claim 45 recites a method for raising antibodies against *Group B Streptococcus*, comprising administering an isolated peptide comprising the amino acid sequence of SEQ ID NO:12 to a patient in need thereof, wherein the peptide is administered in an amount effective to produce the antibodies. Support for claim 45 can be found, for example, at page 2, lines 3-4, 11-16 and 27-30, and page 4, lines 11-15, of the specification.

Claims 25-29 have been objected to for including non-elected subject matter. The applicants elected to prosecute the Group 13 claims, *e.g.*, claims 25-29, drawn to therapy using MS10 peptides. Claims 25, 27, 28, and 32-36 recite administering a bacterial NADP-dependent glyceraldehyde-3-phosphate dehydrogenase. Claims 37-44 recite administering an immunogenically active fragment of a bacterial NADP-dependent glyceraldehyde-3-phosphate dehydrogenase. Claims 45 and 46 recite administering a peptide comprising the amino acid sequence of SEQ ID NO:12. The MS10 peptide (SEQ ID NO:12) is an NADP-dependent glyceraldehyde-3-phosphate dehydrogenase. The applicants respectfully submit that claims 25, 27, and 28, as currently amended, and new claims 32-46 are directed to elected subject matter. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 25-28 have been rejected under 35 U.S.C. §112, first paragraph, as lacking sufficient written description. The applicants respectfully submit that the subject specification provides a sufficient written description of the claimed methods.

Claim 25 has been amended to recite that an isolated bacterial NADP-dependent glyceraldehyde-3-phosphate dehydrogenase is administered to the patient. As indicated in Example

5, at page 10 of the specification, in addition to the GBS MS10 gene product, other glyceraldehyde-3-phosphate dehydrogenases can be identified in *Streptococcus mutans*, *Nicotiana plumb*, *Pisum savitum*, and *Zea mays*, for example. The applicants respectfully submit that one of ordinary skill in the art would appreciate that the applicants were in possession of the glyceraldehyde-3-phosphate dehydrogenases recited in the claims as currently amended. Methods for obtaining homologues and immunogenic fragments of nucleotide sequences and amino acid sequences are well known in the art. For example, as indicated at page 4, lines 1-5 of the specification, other glyceraldehyde-3-phosphate dehydrogenases can be established by searching existing databases, such as the EMBL Nucleotide Sequence Database collaboration or GenBank of the National Center for Biotechnology Information (NCBI).

Claim 37 recites that an immunogenically amount of an isolated peptide is administered to the patient, wherein the peptide is an immunogenic fragment of a bacterial NADP-dependent glyceraldehyde-3-phosphate dehydrogenase. With the benefit of the subject specification, immunogenic fragments of bacterial NADP-dependent glyceraldehyde-3-phosphate dehydrogenases can be obtained by one of ordinary skill in the art. The skilled artisan can determine suitable portions of the polypeptide that retain the immunogenic properties of the native molecule without resort to undue experimentation. Since prior to 1984, it has been well-known that *Bal*31 exonuclease can be conveniently used for time-controlled limited digestion of DNA encoding polypeptides. See for example, Maniatis, *et al.* (1982) *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, NY, pages 135-139. Given any known DNA sequence, the skilled artisan, by using *Bal*31 exonuclease, could easily have removed nucleotides from either or both ends of the DNA molecule to systematically, routinely, and certainly generate a wide spectrum of DNA subsequences from all along the length of the molecule in one afternoon; and then introduce them into host cells. Likewise, successive N-terminal and/or C-terminal degradation of the native polypeptide can be carried out using exoproteases, such as carboxypeptidases. Endoproteases or acids having specific peptide bond cleavage activity can also be used to obtain immunogenic portions that retain the ability to elicit the recited immune response. The immunogenicity of such subsequences can be verified using methods disclosed in the subject application and/or other methods known to those skilled in the art.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claims 25-29 have been rejected under 35 U.S.C. §112, first paragraph, as non-enabled by the specification. The applicants respectfully submit that the claimed invention is fully enabled by the subject specification.

Claims 25 and 37 recite methods for the treatment or prevention of a Group B *Streptococcal* infection. Claim 45 recites a method for raising antibodies against Group B *Streptococcus*.

Submitted herewith for the Examiner's consideration is a Declaration under 37 C.F.R. §1.132 by Joanne Moore, an inventor of the claimed subject matter. The Moore Declaration is submitted herewith to verify the accuracy and sufficiency of what is taught in the specification as originally filed. As indicated, at page 2 of the Declaration, having identified the MS10 protein (SEQ ID NO:12), an NADP-dependent Glyceraldehyde-3-phosphate Dehydrogenase, as being located on the outer surface of a Group B Streptococcal (GBS) microorganism, the protein was tested for its ability to provide a protective effect upon GBS infection. The protein was used to raise anti-sera directed against the protein in rabbits. IgG was then purified from the sera and administered to rat pups, along with PBS (experimental control) and IgG from anti-sera raised against wild-type GBS and other isolated GBS proteins, for comparison. The rat pups were then challenged with the A909 strain of GBS. The results are shown in Table 1 at page 3 of the Moore Declaration and Figure 1 of Exhibit B, which accompanies the Declaration.

As indicated at paragraphs 6 and 7 of the Moore Declaration, the IgG obtained from inoculation with the NADP-dependent Glyceraldehyde-3-phosphate Dehydrogenase showed a significant protective effect compared to the experimental control and an advantageous level of protection compared to other isolated GBS proteins. Based on the experimental data obtained from the MS10 protein, it is reasonable to expect that other NADP-dependent Glyceraldehyde-3-phosphate Dehydrogenases have similar immunogenicity, as taught in the subject specification. Immunogenic fragments of the NADP-dependent Glyceraldehyde-3-phosphate Dehydrogenase would also be expected to have therapeutic utility when administered in immunogenic amounts, as taught in the subject specification.

In view of the guidance provided in the subject specification, and the level of skill of those in the art, one of ordinary skill in the art could carry out the claimed methods without resort to undue experimentation. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph, is respectfully requested.

Claims 25-29 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite. The applicants respectfully submit that the metes and bounds of the claimed subject matter is readily ascertained by those of ordinary skill in the art. However, the applicants have amended the claims to delete the phrase "condition associated with bacterial infection". Reconsideration and withdrawal of the rejection is respectfully requested.

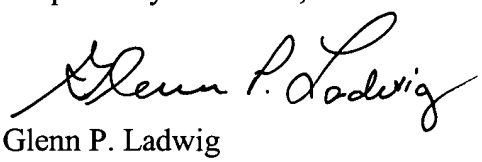
Claims 25-29 have been rejected under 35 U.S.C. §102(b) as being anticipated by Itoh *et al.* (*Microbiol. Immunol.*, 1986, 30(4):297-305). Claims 25-29 have also been rejected under 35 U.S.C. §102(b) as being anticipated by Ichiman *et al.* (*Can. J. Microbiol.*, 1982, 28:726-732). As discussed during the telephonic interview, claims 25, 27, 28, and new claims 32-46 recite that the NADP-dependent glyceraldehyde-3-phosphate dehydrogenase, or immunogenic fragment thereof, which is administered to the patient, is isolated. Support for this amendment can be found, for example, at page 2, lines 15-16, and page 4, lines 6-7, of the subject specification. In contrast, the Itoh *et al.* and Ichiman *et al.* publications describe whole cell vaccines comprising Group B *Streptococci*. Therefore, the cited references do not teach or suggest administration of an isolated NADP-dependent glyceraldehyde-3-phosphate dehydrogenase (such as MS10 (SEQ ID NO:12)), or an immunogenic fragment of an NADP-dependent glyceraldehyde-3-phosphate dehydrogenase. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b) is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Declaration under 37 C.F.R. 1.132 by Joanne Moore
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